DATE: **April 7, 1999**

MEMORANDUM

SUBJECT: **Phostebupirim (129086): HIARC reevaluation of acute dietary RfD**

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THROUGH: Alan Nielsen, Branch Senior Scientist
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1. Recommendation to the HIARC: The Hazard Identification Assessment Review Committee (HIARC) met on March 25, 1999 to evaluate the impact that the results of acute (MRID No. 43473001) and subchronic (MRID: 43656302) neurotoxicity studies in the rat would have on risk assessment endpoints. After reviewing the data, the HIARC agreed that the acute dietary endpoint should be based on the acute neurotoxicity study, and further, because the data gap for the two neurotoxicity studies was fulfilled, the 3X FQPA safety factor should be removed. The Committee felt that the acute (single dose) study was a more realistic exposure scenario than the previous developmental study in the rabbit study. The following endpoint and doses for acute assessment are summarized in the following table.

Dose and Endpoint Selected for Acute Dietary Risk Assessment

Critical Study	Acute Neurotoxicity Study in the Rat (MRID 43473001)
Endpoint	Plasma and RBC ChEI [a] at 1.5 hr post-dosing
NOAEL	0.5 mg/kg (LOAEL) NOAEL not achieved in males
Uncertainty Factor	UF= 300 100X for inter- and intraspecies variation and 3X for lack of NOAEL
RfD	0.002 mg/kg
FQPA Safety Factor	1 (FQPA factor removed)
aPAD [b]	0.002 mg/kg (Same as acute RfD)

a ChEI = Cholinesterase Inhibition

b aPAD = Acute Population Adjusted Dose = $\frac{\text{Acute RfD}}{\text{F QPA Safety Factor}}$

cc Christina Jarvis (HED/RRB II, 7509C)
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Jacqueline McQueen (SRRD, 7508W)